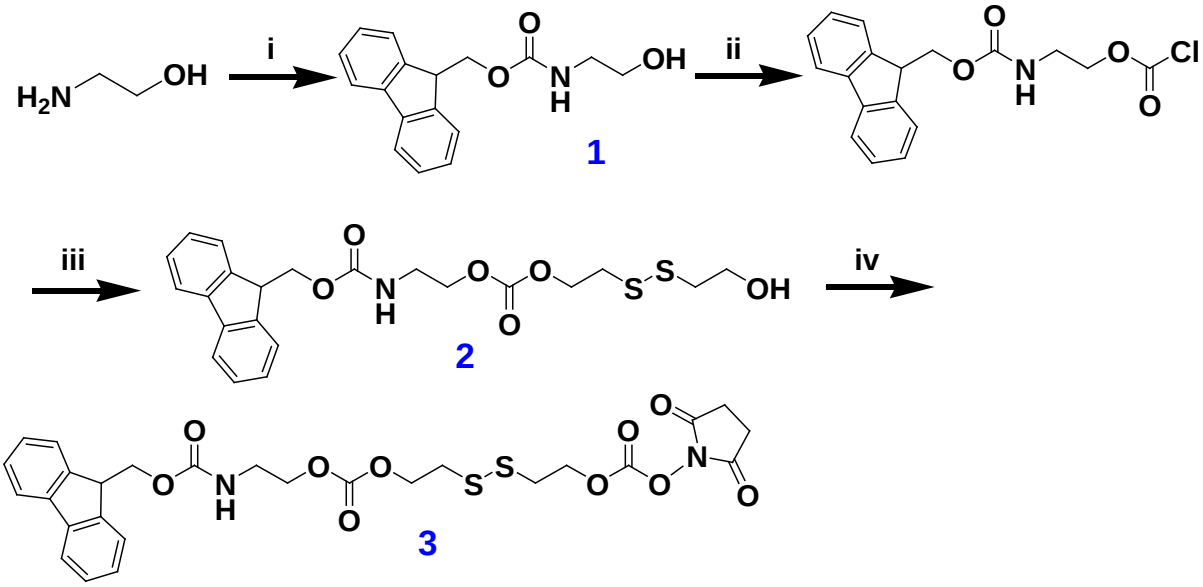
Supporting Information

Materials and general methods:

Chemicals: Fmoc-amino acids were obtained from GL Biochem (Shanghai). Triphosgene was obtained from Aladdin (Shanghai). All the other starting materials were obtained from *Alfa*. Commercially available reagents were used without further purification, unless noted otherwise. Nanopure water was used for all experiments. All other chemicals were reagent grade or better.

Syntheses and characterizations:



i) Fmoc-OSu, Acetone; ii) $(CCl_2O)_3$, 1.3eq DMAP, DCM;
iii) $C_4H_{10}S_2O_2$, 1eq DMAP, DCM
iv) 2eq DSC, 3eq Triethylamine, Acetonitrile

Scheme S-1. Synthetic pathway for the preparation of disulfide bond containing **3** for solid phase peptide synthesis

The synthesis of 3 was described in Scheme S-1.

Preparation of Compound 1: To a 100 mL acetone solution containing 3.38g (10 mmol) of Fmoc-OSu, 600 uL of ethanolamine (10 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 2 hours. And then it was concentrated by a rotary evaporator. The pure product of **1** was obtained as solid form by flash chromatography using ethyl acetate and ether as eluents. (yield = 60%). ^{1}H-NMR (300 MHz, DMSO-d6) δ 7.814-7.887 (m, 4H), 7.302-7.429 (m, 5H), 6.532(s, 1 H), 6.273(s, 2H), 3.339-3.381 (t, 2H), 2.953-3.010 (d, 2H), 2.679(s, 1 H). MS: calc. M^+ = 283.1, obsvd. $(M+Na)^+$ =306.3.

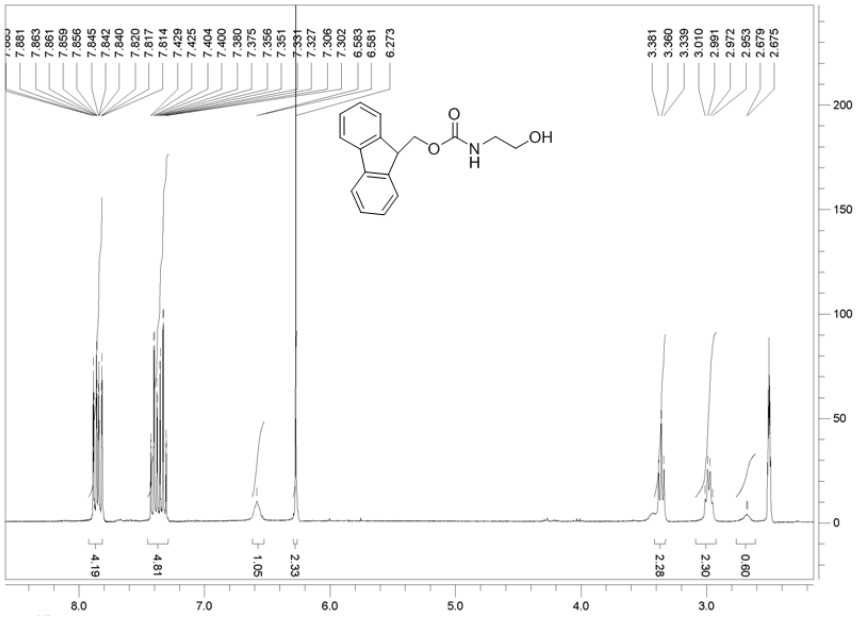


Fig. S-1. ^{1}H-NMR of compound **1**

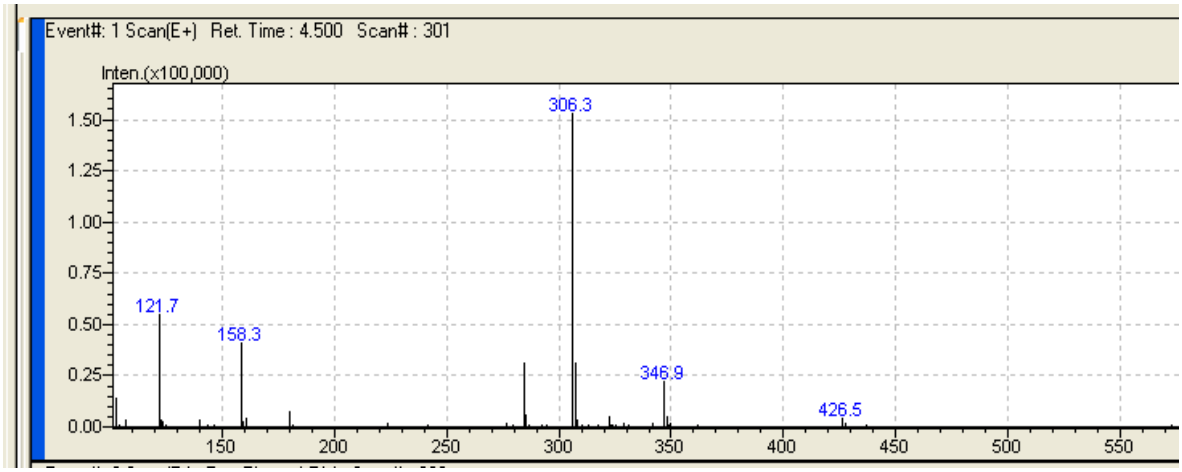


Fig. S-2. MS spectrum of compound **1**

Preparation of Compound 2: to a solution of 20 mL DCM containing 0.312g (1.05 mmol) of triphosgen, a 20 mL DCM solution containing 0.85g of 1 (3.0 mmol) and 0.366g of DMAP (3.0 mmol) was added dropwise at 0 ^{0}C (ice bath) and N_2 atmosphere. The reaction mixture was stirred for another one hour at 0 ^{0}C and then at room temperature overnight.

To the above reaction mixture, a 40 mL DCM solution containing 480 uL (3.9 mmol) of 2-hydroxyethyl disulfide and 0.476g (3.9 mmol) of DMAP was added dropwise at 0 ^{0}C. The resulting mixture was stirred overnight. The pure compound 2 was obtained as viscous liquid after flash chromatography using ether and ethyl acetate as eluents. (yield = 70%). ^{1}H-NMR (300 MHz, DMSO-d6) δ7.818-7.864 (m, 3H), 7.666 (d, 1H), 7.403-7.642(m, 1H), 7.309-7.382(m, 3H), 6.850(t, 1H), 6.243(s, 1H), 4.261-4.303(t, 2H), 4.027-4.064(t, 2H), 3.579-3.622(t, 2H), 3.318-3.388(m, 2H), 3.120-3.200(m,

1H), 2.923-2.987(m, 2H), 2.747-2.811(t, 2H), 1.047-1.093(t, 2H). MS: calc. M^+ = 463.1, obsvd. $(M+Na)^+$ =485.1.

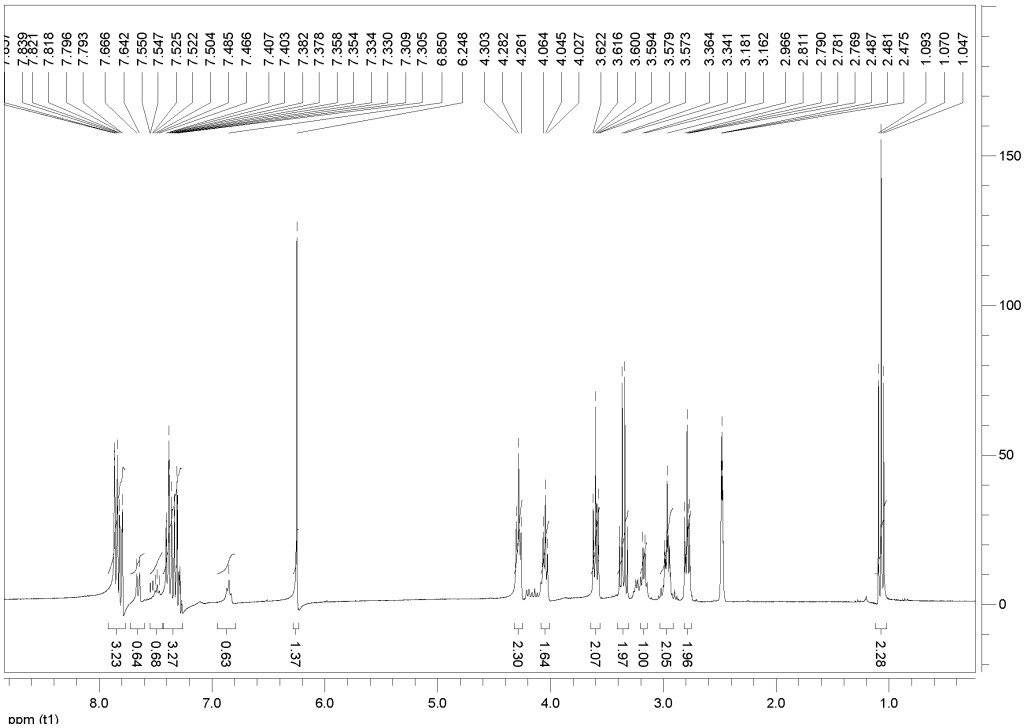


Fig. S-3. ^{1}H-NMR of compound **2**

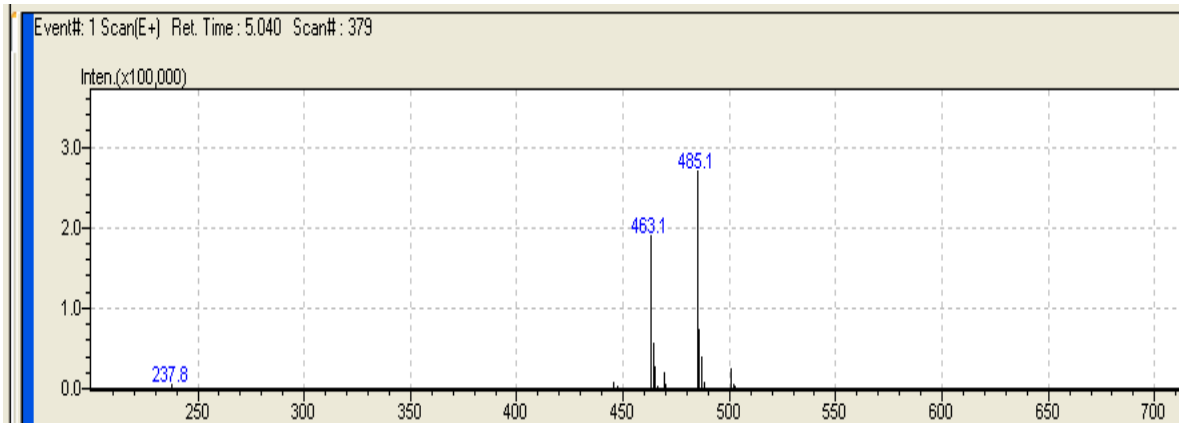


Fig. S-4. MS spectrum of compound **2**

Preparation of Compound 3: To a 100 mL acetonitrile containing 1.8 mmol of 2, 0.922g (3.6 mmol) of DSC was added. After being stirred at room temperature for 5 minutes, 777.6 uL (5.4 mmol) of diethylamine was added in N_2 atmosphere. The reaction mixture was stirred at room temperature for 4 hours and then concentrated by rotary evaporator. The crude product of **3** was kept in a -20 ^{0}C fridge and used directly for SPPS. MS: calc. M^+ = 602.6, obsvd. $(M+H)^+$ = 603.6, $(M+Na)^+$ =625.7

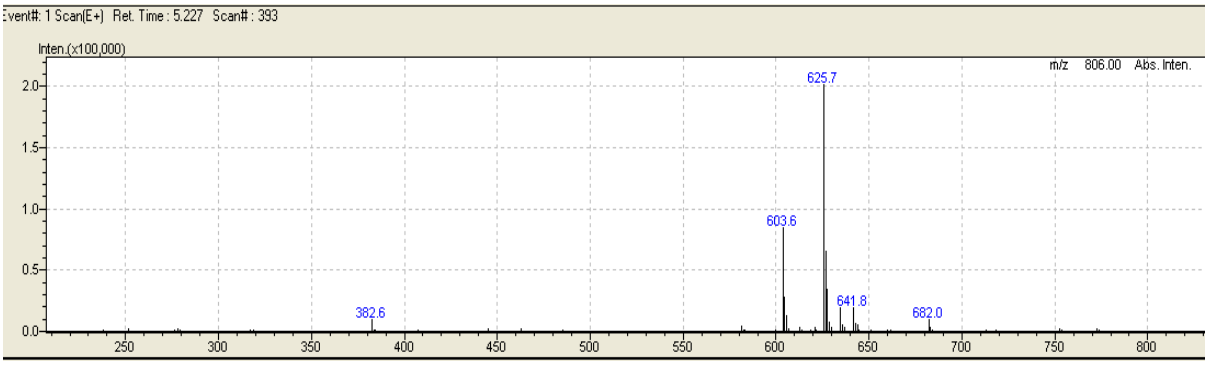


Fig. S-5. MS spectrum of compound **3**

Preparation of compound 4: The compound **4** was prepared by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin, the corresponding N-Fmoc protected amino acids with side chains properly protected by a tert-butyl group and compound **3**. The first amino acid of Fmoc-Glycine was loaded on the resin at the C-terminal with the loading efficiency of about 0.8 mmol/g in anhydrous dichloromethane (DCM). After 1 hours, the reaction solution was drained and the resin was washed by dimethyl Formamide (DMF) for 5 minutes. The un-reacted reactive group on resin was capped by a solution containing DCM:MeOH:DIPEA = 17:2:1 for 10 minutes. Afterwards, 20% piperidine in DMF was used to deprotect Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group on the resin using HBTU as the coupling reagent and DIPEA as the catalytic agent. The growth of the peptide chain was according to the established Fmoc SPPS protocol. After the last coupling step, excessive reagents were removed by DMF washing one time for 5 minutes (5 mL per gram of resin), followed by five steps of washing using DCM for 2 min (5 mL per gram of resin). The peptide conjugates were cleaved from resin using 1% of TFA in DCM for 10 times (each time for 1 minute). After combining these solutions together and concentrated by the rotary evaporator, diethyl ether was then added to afford the crude product in solid form. The resulting precipitate was centrifuged for 10 min at room temperature at 10,000 rpm and further purified by reverse phase HPLC. ^{1}H NMR (300 MHz, DMSO-d6) δ 8.328-8.396 (m, 2H), 8.188-8.230 (t, 1H), 8.112-8.171 (m, 4H), 8.000-8.027 (d, 1H), 7.777-7.854 (m, 4H), 7.721 (s, 1H), 7.407-7.481 (m, 4H), 7.226-7.245 (t, 4H), 7.114-7.187 (m, 10H), 4.463-4.595 (m, 5H), 4.151-4.192 (t, 4H), 4.020-4.057 (t, 2H), 3.843-3.865 (m, 2H), 3.717-3.754 (m, 6H), 3.569-3.642 (m, 5H), 3.156-3.240 (m, 3H), 2.840-2.943 (m, 6H), 1.190-1.246 (m, 1H). MS: calc. M^{+} = 1179.4, obsvd. $(M+NH_4)^{+}$ =1197.4372.

Fig. S-6. ^{1}H NMR of compound **4** (the peak at about 1.1 ppm was from unknown impurity)

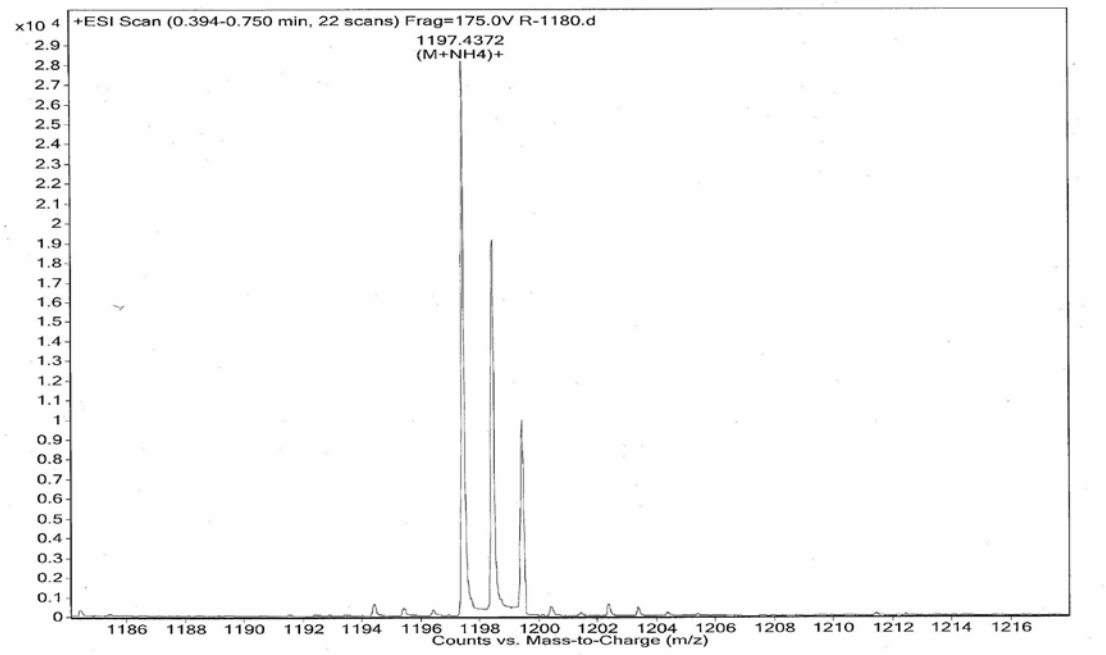


Fig. S-7. HR-MS of compound **4**

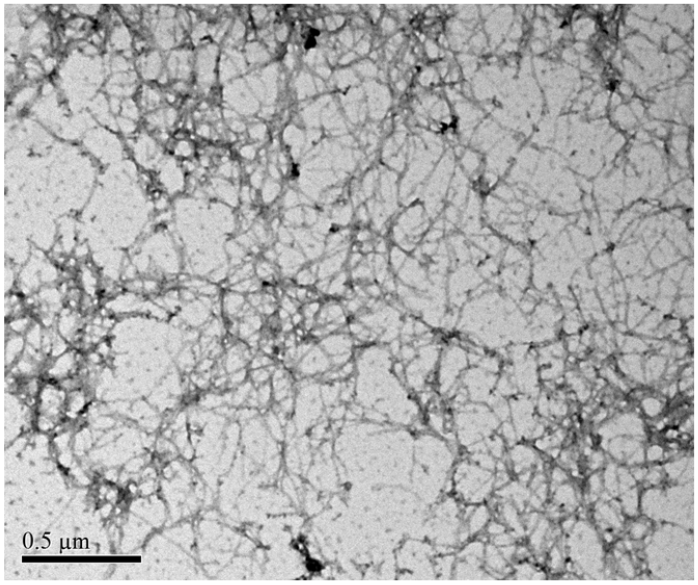


Fig. S-8. The TEM image of a gel at 120h time point

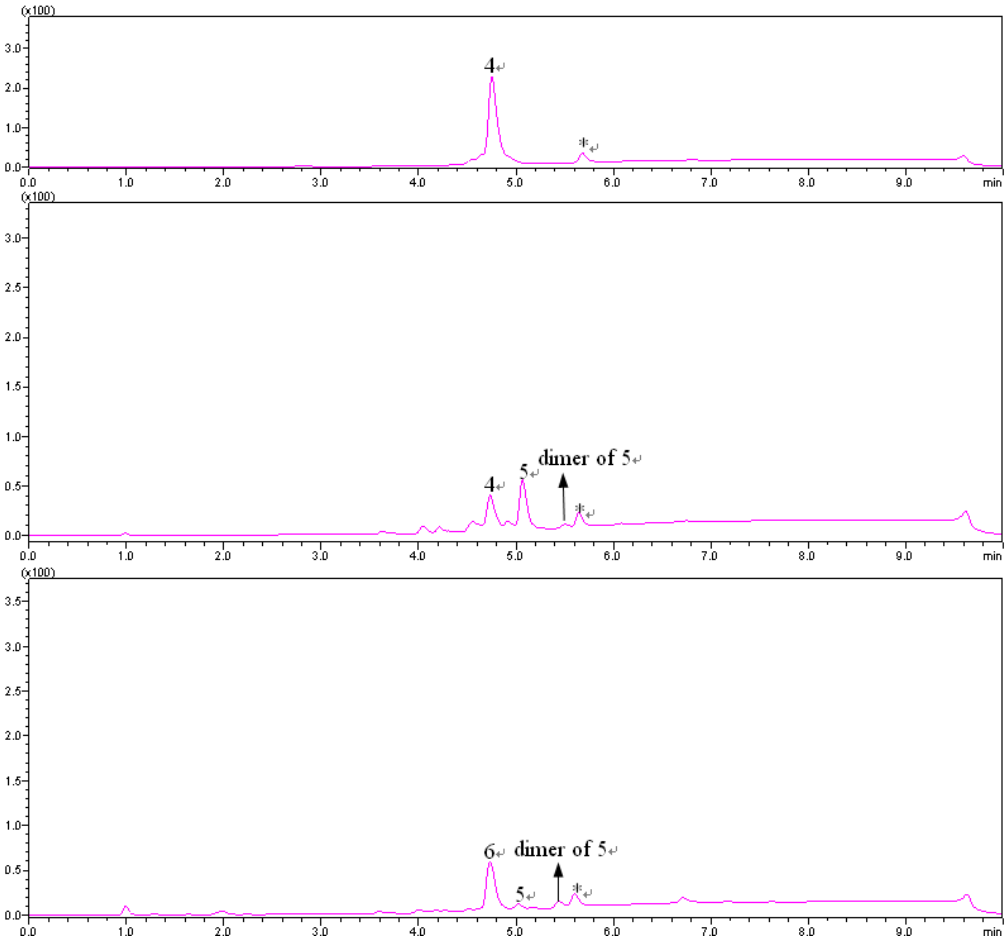


Fig. S-9. LC-MS spectra of top) compound 4, middle) gel at gelling point